510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:
K052346

B. Purpose for Submission:
For addition of Penicillin G on the MicroScan® Synergies plus™ Gram-Positive MIC/Combo Panels for testing appropriate *Staphylococcus* spp and *Enterococcus* spp

C. Measurand:
Penicillin (0.03 – 4 µg/mL for *Staphylococci* and 0.5 – 64 µg/mL for *Enterococci*)

D. Type of Test:
Quantitative and Qualitative growth based detection algorithm using optics light detection

E. Applicant:
Dade Behring Inc, MicroScan®

F. Proprietary and Established Names:
MicroScan® Synergies plus™ Gram-Positive MIC/Combo Panels

G. Regulatory Information:

1. Regulation section:
   866.1645 - Fully automated short-term incubation cycle antimicrobial susceptibility system
   866.1640 - Antimicrobial Susceptibility Test Powder

2. Classification:
   Class II

3. Product code:
   LON – Automated AST system short incubation
   LRG-Instrument for Auto Reader & Interpretation of Overnight Antimicrobial Susceptibility Systems
   JWY - Manual Antimicrobial Susceptibility Test Systems
   LTT – Panels, Test, Susceptibility, Antimicrobial

4. Panel:
   83 Microbiology

H. Intended Use:

1. Intended use(s):

   Penicillin at concentrations of 0.03 to 4 µg/mL for *Staphylococci* and 0.5 to 64 µg/mL for *Enterococci* on the MicroScan® Synergies plus ™ Gram-Positive MIC/Combo Panel is intended for use with MicroScan® Synergies plus™ Panels read on the WalkAway® -SI System (including upgraded WalkAway® -40 or WalkAway® -96 to meet WalkAway® SI equivalence).

   MicroScan® panels are designed for use in determining quantitative and/or qualitative antimicrobial agent susceptibility and/or identification to the species level of colonies, grown on solid media, of rapidly growing aerobic and facultative anaerobic gram-positive cocci and Listeria.

2. Indication(s) for use:
   The addition of penicillin at concentrations of 0.03 to 4 µg/mL for testing *Staphylococci* and 0.5 to 64 µg/mL for testing *Enterococci* to the gram-positive test panel at 4.5-16 hours or 16-20 hours for an overnight reading.

3. Special conditions for use statement(s):
   - Turbidity method of inoculum preparation only.
   - For prescription use only.
   - *S. saprophyticus* will not be reported

4. Special instrument requirements:
   Not Applicable

I. Device Description:

Each panel contains two control wells: a negative control well, and a growth control well (contains test medium without antibiotic). Antibiotics are diluted in water, buffer, or minute concentrations of broth to selected concentrations prior to dehydration of the panels. The panel is rehydrated and inoculated at the same time with 0.1 ml of suspension prepared by the turbidity method (inoculum prepared in 0.4% saline with PLURONIC®, then 0.1ml transferred to 25ml of inoculum Synergies plus Pos Broth with PLURONIC®) for a final inoculum concentration of 3-7 X 10^5 CFU/ml. Panels are incubated in a Walk-Away® System and read periodically starting at 4.5 hours until sufficient growth to determine the MIC. Alternately the panels may be incubated at 35^o C in a non-CO_2 for 16-24 hours and read by visual observation of growth.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   MicroScan® Dried Gram-Positive and Gram-Negative MIC/Combo Panels

2. Predicate 510(k) number(s):
   k862140
   k020185

3. Comparison with predicate:

Similarities		
Item	**Device**	**Predicate**
Intended use	MicroScan® panels are designed for use in determining quantitative and/or qualitative antimicrobial agent susceptibility and/or identification to the species level of colonies, grown on solid media, of rapidly growing aerobic and facultative anaerobic organisms	Same
Specimen	Isolated colonies from culture used	Same
Inoculum	Inoculum density to 0.5 McFarland standard	Same
Incubation	<16 hours 16 – 24 hours	Same
Results	Quantitative with qualitative interpretations	Same
Technology	Growth based	Same

Differences		
Item	**Device**	**Predicate**
Panels	Dried penicillin in water	Dried clindamycin or gentamicin in broth
Reading	Uses both an early read and overnight methods in the same system	Overnight system uses only the overnight reading methods and <16 hour instruments use only the <16 hour read methods.
Inoculum preparation	Turbidity method of inoculation only.	Inoculum prepared from isolated colonies using either the Turbidity method or Prompt® system
Instrument	WalkAway® -SI System or equivalent	autoScan® -4 or WalkAway®
Antibiotic	Penicillin 0.03 – 4 µg/mL for *Staphylococci* 0.5 – 64 µg/mL for *Enterococci*	Different concentrations depending on the antibiotic

K. Standard/Guidance Document Referenced (if applicable):

Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA"; Clinical and Laboratory Standards Institute (CLSI) M7 (M100-S15) "Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard".

L. Test Principle:

The WalkAway® SI uses a Colorimetric Optics System consisting of a color wheel/lamp assembly and a Photosensor. There is an initial read at 2.5 hours with a possible final read at 4.5, 5.5, 6.5, 8, 12, 16, or 18 hours (overnight instrument readings, manual readings) depending on the growth rate of the organism being tested. The time of final read is dependent on the growth rate of the organism and the sensitivity of the automatic reader since cell densities below 2×10^7 cells/ml are not detected.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. *Precision/Reproducibility:*
   Reproducibility was demonstrated using 20 isolates tested at 3 sites on 3 separate days in triplicate. The study included the testing on the WalkAway® SI read at <16 hours, WalkAway® 16-18 hour readings and manual readings at 16-20 hours incubation. The WalkAway® SI had 3 results that were not readable at ≥16 hours. All results were >95% reproducible.

   b. *Linearity/assay reportable range:*

   Not Applicable

   c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

   The recommended QC isolates, *E. faecalis* ATCC 29212 and *S. aureus* ATCC 29213 were tested a sufficient number of times with acceptable results on all testing days with the reference method. The reference and the three different read methods had the same mode with *E. faecalis* ATCC 29212. However, the mode of the reference method was different from the 3 different read methods with the *S. aureus* ATCC 29213 but still within essential agreement therefore this QC is acceptable. The main purpose of the *S. aureus* ATCC 29213 QC organism is to demonstrate that it is a penicillinase producer with an expected range of ≥0.25. *E. faecalis* 29212 appears to be a better indicator of the activity of penicillin.

Quality control results demonstrated the ability of the different reading parameters (manual and instrument) to produce acceptable results.

The following table provides the frequency of the results in each concentration with the expected range stated.

			Results		
Organism	Conc in µg/mL	# reference	MicroScan®		
			Manual overnight	Instrument overnight	Synergies Plus
E .faecalis ATCC 29212 Expected Range: 1 – 4 µg/mL	1	83	83	84	81
	2	3	3	2	5
S. aureus ATCC 29213 Expected Range: 0.25 – 2 µg/mL	0.25	2			
	0.5	39	1		
	1	28	27	27	51
	2	12	26	25	18
	4	4	22	24	14
	>4		9	9	2

Inoculum density control: A turbidity meter was used for the turbidity inoculation method.

d. Detection limit:
Not Applicable

e. Analytical specificity:
Not Applicable

f. Assay cut-off:
Not Applicable

2. Comparison studies:

a. Method comparison with predicate device:
Clinical testing was conducted at 3 sites using fresh isolates supplemented with stock isolates. A total of 534 gram-positive isolates were tested of which 469 were fresh isolates and 65 were stock isolates. There were 138 challenge isolates tested at one site and compared to the reference broth dilution result mode that was determined by previous testing of each isolate multiple times in the recommended reference panel. The Synergies plus™ readings were obtained at times between 4.5 and 16 hours of incubation for > 99% of the results. An additional comparison was done with readings on the instrument after overnight incubation and also read manually when incubated 16- 18

hours. Performance by these alternate reading methods was also acceptable with no apparent differences or trends. The recommended CLSI reference method was followed with the exception of the use of a small amount (0.1%) PLURONIC® in the final inoculum. A validation of the use of PLURONIC® in the frozen reference panels was conducted. Similar calculations for the different reading methods were performed with very little difference. The test device had a no growth rate of <10%.

The charts below demonstrated the performance of all three reading methods (Synergies plus™ readings at <16 hours, overnight on the WalkAway® and manually read at 18 hours using the touchScan®-SR) when compared to the reference method.

Summary Table for the Rapid Instrument Read

	Total	**EA**	**%EA**	**Total evaluable**	**EA of evaluable**	**%EA**	**CA**	**%CA**	**#R**	**min**	**maj**	**vmj**
Efficacy	530	487	91.9	254	238	93.7	525	99.1	325	N/A	3	2
Challenge	138	133	96.4	62	58	93.5	136	98.6	90	N/A	1	1
Combined	668	620	92.8	316	296	93.7	661	99.0	415	N/A	4	3

Summary Table for the Overnight Instrument Read

	Total	**EA**	**%EA**	**Total evaluable**	**EA of evaluable**	**%EA**	**CA**	**%CA**	**#R**	**min**	**maj**	**vmj**
Efficacy	534	518	97.0	251	236	94.0	531	99.4	325	N/A	3	0
Challenge	138	137	99.3	64	63	98.4	138	100	90	N/A	0	0
Combined	672	655	97.5	315	299	94.9	669	99.6	415	N/A	3	0

Summary Table for the Overnight Manual Read

	Total	**EA**	**%EA**	**Total evaluable**	**EA of evaluable**	**%EA**	**CA**	**%CA**	**#R**	**min**	**maj**	**vmj**
Efficacy	534	519	97.2	249	235	94.4	532	99.6	325	N/A	2	0
Challenge	138	137	99.3	64	63	98.4	138	100	90	N/A	0	0
Combined	672	656	97.6	313	298	95.2	670	99.7	415	N/A	02	0

EA-Essential Agreement
CA-Category Agreement
R-resistant isolates
maj-major discrepancies
vmj-very major discrepancies
min- minor discrepancies
NA – No intermediate range therefore no minor errors possible

Evaluable results are those that fall within the test range of the reference method and could also be on-scale with the new device if within the plus/minus one dilution variability. EA is when there is agreement between the reference method and the MicroScan® within plus or minus one serial two-fold dilution of antibiotic. CA is when the interpretation of the reference method agrees exactly with the interpretation of the MicroScan® result.

A slight trend was observed where the *S. aureus* in the QC and efficacy studies was more resistant in the test method than the reference method but still in essential agreement. This trending was observed in all three read methods.

b. Matrix comparison:
Not Applicable

3. Clinical studies:

a. Clinical Sensitivity:
Not Applicable

b. Clinical specificity:
Not Applicable

c. Other clinical supportive data (when a. and b. are not applicable):
Not Applicable

4. Clinical cut-off:
Not Applicable

5. Expected values/Reference range:
Staphylococcus spp. ≤0.12 (S), ≥0.25 (R)
Enterococcus spp. ≤8 (S), ≥16 (R)

The interpretative criteria and Quality Control Ranges are the same as recommended in the CLSI. All values are included in the package insert.

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.